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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/983,025	10/22/2001	Claus Oxvig	OXVIG=1A	7756

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BROWDY AND NEIMARK, P.L.L.C.  
624 Ninth Street, N.W.  
Washington, DC 20001

EXAMINER

RAMIREZ, DELIA M

ART UNIT PAPER NUMBER

1652

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	Application No. 09/983,025	Applicant(s) OXVIG ET AL.	
	Examiner Delia M. Ramirez	Art Unit 1652	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 05 January 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: see attached. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☒ Applicant's reply has overcome the following rejection(s): see attached.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: none.  
Claim(s) objected to: 70,85,87 and 94.  
Claim(s) rejected: 12,17-19,75,83,90-93 and 95-100.  
Claim(s) withdrawn from consideration: 30-47,49-52,55-58 and 62.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_  
13. ☐ Other: \_\_\_\_\_.

***ADVISORY ACTION***

1. Claims 12, 17-19, 30-47, 49-52, 55-58, 62, 70, 75, 83, 85, 87 and 90-100 are pending.

2. Applicant's submission of a new sequence listing and amended Figure 3 is acknowledged.

Applicant's remarks indicating the reasons why a new sequence listing was needed and how Figure 3 was amended have been fully considered. The new sequence listing and amended drawing have been entered.

3. The request for entering amendments to claims 12, 30, 49, 55, 62, 70, 75, 83, 90-93, 95-100, adding claims 101-102, canceling claims 17, 85, 94, and arguments filed on 1/5/2005 under 37 CFR 1.116 in reply to the Final Action mailed on 9/7/2004 are acknowledged. The proposed amendments to the claims will not be entered. While amendments to the claims seem to overcome the objections, the 35 USC 112, second paragraph rejections, some of the grounds of rejection previously applied in regard to 35 USC 102(a), and some of the grounds of rejections previously applied in regard to 35 USC 112, first paragraph, the proposed amendments to the claims raise new issues which would require further consideration as discussed below.

4. Applicants request that the finality of the previous Office Action be withdrawn since the Examiner did not give patentable weight to certain limitations in claim 95, and therefore, was not properly examined. Applicant's arguments have been fully considered but are not deemed persuasive. The Examiner did not give patentable weight to certain limitations in claim 95 in view of the fact that the claim as written by Applicants was deemed indefinite. However, to further advance prosecution, the Examiner provided an interpretation for that claim even though it was considered indefinite, so that the claim could be examined on the merits, and also provided suggestions as to how it had to be amended, as admitted by Applicants. The Examiner will always try to use the best possible interpretation of an indefinite claim in light of the specification, however, in the instant case, the recitation of consensus sequences without a sequence identifier made it impossible for the Examiner to do a meaningful search. Thus, no patentable weight could be given to those terms.

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5. Proposed amended claims 12, 97-99 would be rejected under 35 USC 112 second paragraph due to the recitation of “iii) competes with mature PAPP-A2” for the following reasons. The term is unclear since one cannot determine if the intended mature PAPP-A2 is one from any source, or if the intended mature PAPP-A2 is a polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2. It is noted that item ii) does not equate the term “mature PAPP-A2” with a particular fragment of the polypeptide of SEQ ID NO: 2, as is the case, for example, in claim 90, item 1(b). Instead, item ii) limits a generic term, i.e. mature PAPP-A2, to a particular fragment of SEQ ID NO: 2, such that the recitation of the term in item iii) does not necessarily imply that the term only encompass that particular fragment of SEQ ID NO: 2. It is suggested that if the intended “mature PAPP-A2” in item iii) is a fragment consisting of residues 234-1791 of SEQ ID NO: 2, the claim be amended to recite “competes with a polypeptide consisting of amino acids 234-1791 of SEQ ID NO: 2 (mature PAPP-A2)”, or similar. For claim interpretation, the suggested language is being used.

6. Proposed amended claims 12, 75, 83, 97-99 would remain rejected and new claim 102 would be rejected under 35 USC 112, first paragraph, as failing to comply with the written description and enablement requirements. In regard to the lack of written description, Applicants argue that (1) claims 97-99 are drawn to precursors of mature PAPP-A2, (2) all of the alternative functions recited in claim 12 are taught in the specification, and (3) there are several species disclosed in the specification which provide adequate description of the genus. In regard to the enablement rejection, Applicants argue that the claimed polypeptides only require one of the recited functions, which is sufficient to confer utility. Applicants also submit that the specification teaches the regions most likely to mediate activity, and that even if some species are inoperative, only those which display the required function are encompassed by the claims.

Applicant's arguments have been fully considered but are not deemed persuasive. The Examiner acknowledges the teachings of the specification and the amendments to the claims. However, the

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Examiner disagrees with Applicant's contention that the claimed invention is adequately described or fully enabled by the teachings of the specification. Amended claim 12, 75 and 83 are still directed to a genus of polypeptides having 97% sequence identity to the polypeptide of SEQ ID NO: 2 wherein said polypeptides can have any biological function due to the recitation of the term "and/or" recited immediately after the functional limitation of item i). It is noted that a genus of proteins which can be recognized by an antibody or compete for binding to an undefined cell surface receptor may potentially have many different biological functions. There is no teaching in the specification as to which antibodies or receptors would recognize/bind a protein which is 97% sequence identical to amino acids 234-1791 of SEQ ID NO: 2 and also has proteolytic activity for IGFBP-5. Also, it is noted that claims 97-99 now recite "wherein said polypeptide or a cleavable fragment corresponding to sequence (II) of said polypeptide". Therefore the limitations recited in i)-iii) are not required for the polypeptide being claimed. All that is required is that a fragment of the polypeptide recited in (II) meets those limitations. As such, the claimed polypeptides may have any function. In addition, the specification discloses one biological function, i.e. proteolytic activity specific for IGFBP-5, therefore one cannot reasonably conclude that the claimed genus is adequately described.

In regard to the enablement rejection, it is noted that while the polypeptides of claims 97-99 can have any biological function, the specification does not provide the functions of all the polypeptides claimed. In addition, as indicated above, a genus of proteins which can be recognized by an antibody or compete for binding to a cell surface receptor may potentially have many different biological functions. As indicated above, no teaching has been provided as to the required characteristics in an antibody or receptor such that the protein they bind is 97% sequence identical to amino acids 234-1791 of SEQ ID NO: 2 and has proteolytic activity for IGFBP-5. Contrary to Applicant's assertion, being recognized by an antibody or being able to bind an undefined cell surface receptor does not meet the utility requirement since those uses are neither specific and substantial or well-established. It would require undue

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experimentation to determine a specific and substantial use for the claimed polypeptides. Therefore, one cannot reasonably conclude that the claimed invention is fully enabled by the specification.

7. Proposed amended claims 12, 75 and previously presented 18-19 (dependent upon claim 12) would remain rejected under 35 USC 102 (a) as being anticipated by Farr et al. Applicants argue that the % identity calculation should take into consideration the portion of Farr's protein which corresponds to amino acids 168-233 of SEQ ID NO: 2 as mismatches, and that the longer sequence (1624 amino acids long by Farr et al.) should be used. Applicants also submit that the claims previously directed to specific fragments have been amended such that they are no longer anticipated by the instant reference.

Applicant's arguments have been fully considered but are not deemed persuasive. Claim 12 recites "at least 97% identical to the polypeptide of (a), (b) or (c)". Thus, claims 12, 18-19 and 75 are directed to a polypeptide at least 97% sequence identical to amino acids 234-1791 of SEQ ID NO: 2. In view of the fact that the identity recited is in reference to amino acids 234-1791 of SEQ ID NO: 2, the calculation should take in consideration only that which is being recited, which in this case is amino acids 234-1791 of SEQ ID NO: 2. The region in the polypeptide of Farr et al. which is not corresponding to what is being recited should not be part of the calculation. The 4 mismatches previously indicated are within the region recited and have been taken into account. As discussed in previous Office Actions, the polypeptide of Farr et al. is 99.7% sequence identical to the polypeptide of SEQ ID NO: 2, therefore anticipating the instant claims as written.

In regard to claims directed to fragments, i.e. amended claims 90-92 and 96, the claims as amended require the presence of regions of SEQ ID NO: 2 which contain cysteine residues not taught or suggested by Farr et al. Therefore, these claims would be free of the prior art as written.

8. Proposed amended claims 70, 87, 90-93, 95-96, and new claim 101 would be allowable over the prior art of record but would be objected to since they depend upon rejected base claims.

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9. The rejections previously applied are, therefore, maintained for the reasons of record in view of the non-entry of the proposed amendments.

10. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: NONE

Claims(s) objected to: 70, 85, 87 and 94

Claim(s) rejected: 12, 17-19, 75, 83, 90-93 and 95-100

Claim(s) withdrawn from consideration: 30-47, 49-52, 55-58, 62

11. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.


12. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

DR  
February 7, 2005

  
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